31. (New) The method of claim 5, wherein said multivalent polypeptide is used in an ELISA format.

32. (New) The method of claim 6, wherein said target polypeptide is purified from the reaction mixture to a composition that is more than 90% pure.

33. (New) The method of claim 5, wherein said reaction mixture is semi-solid

34. (New) The method of claim 12, wherein said multivalent polypeptide is used in an ELISA format.

35. (New) The method of claim 12, wherein said target polypeptide is purified from the reaction mixture to a composition that is more than 90% pure.

36. (New) The method of claim 12, wherein said reaction mixture is semi-solid.

Please also see a Claims Appendix with a complete listing of the claims as amended without correction marks.

REMARKS

The Office Action dated February 7, 2003 has been carefully reviewed. Applicants would like to thank the Examiner for considerate approach to the last Applicant response and to acknowledge the withdrawal of several grounds of rejection of the amended claims. In the instant case claims 5, 6 8-10, 12-14 and 19-36 are pending. Claim 15 has been cancelled. Claims 5, 9-10, 12, 22, 25 and 27-28 have been amended. Claims 31 through 36 have been added.

Reconsideration of the previous claim rejections is respectfully requested. Applicants thank the Examiner for her thorough and detailed remarks attached to the most recent Office Action.

Applicants believe that the amendments which have been made, along with the extensive nature of this response serve to put all the remaining claims in better condition for allowance. This is also true with respect to the canceled claims as well as with the claims which were amended or added. Given the above, it is specifically and respectfully requested that the Examiner enter and allow the claims as amended herein.

Election/Restriction

In her latest Office Action the Examiner maintained and made final her Restriction Requirement regarding examination of the claims as filed. Respectfully, though withdrawn from further consideration in this case, those claims not elected by the Applicant, and pending in the current case, are not cancelled or abandoned, and remain part of the application pending a successful appeal to the Board of Patent Appeals regarding the restriction requirement, or their inclusion in a new application as a divisional action to the current case.

Claim Amendments

Applicants wish the Examiner to take note that their representation before the USPTO has recently changed. This change in representation has necessitated a review of the specification and prior prosecution activities by their new attorney. During this review it was determined that substantial amendments to the claims were needed to answer the Examiner's objections and to more fully present the invention for examination. Therefore each of the pending independent claims has been amended or has been added by Applicant in this Response. The pending claims as a whole, as provided by Applicant, are thus intended to be both part of a fully responsive reply to the Examiner's rejections and fully grounded in the teachings of the specification. MPEP §§ 608.01; 714.

Clarification of Rejection

It should be noted that in the Office Action of February 7, 2003 (page 3, 4th paragraph under the 35 USC § 112 Rejections) provided by the Examiner, the Examiner rejected claims 9, 10, 20-22,26-28 under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey that the Applicants had possession of the invention at the time of filing. Respectfully, Applicant can find no specific basis for this rejection in the text of the Office Action. Therefore it is unclear whether the Examiner provided this rejection broadly to the pending claims *in toto* or this rejection was in fact further discussed by the Examiner in other rejections of a similar set of claims later in the Office Action. [*See*, Claims 9, 10, 21, 22, 27 and 28 rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the Applicants, at the time the application was filed, had possession of the claimed invention – below].

Applicants respectfully request that the Examiner provide a basis for this rejection to which they may answer and hopefully traverse or amend the affected claims in compliance with a fully presented rejection.

However, in an effort to expedite the prosecution of this case Applicant has assumed that the §112, first paragraph, rejection provided by the Examiner in the February 7, 2003 Office Action to claims 9, 10, 20-22,26-28 under 35 U.S.C. § 112, first paragraph focuses on the use of certain types of molecules or polypeptide moieties in the noted claims. Applicants, note that these claims recite the binding regions of polypeptides derived from protein L, or the cellulose binding domain (CBD) or chemically functional fragments thereof. These proteins were known by artisans in the field at the time of filing and their pharmacological, chemical, and/or molecular activities were also known.

Moreover, regarding the rejected claims, the Examiner previously rejected claims 9 and 10 asserting that the term 'a fragment thereof' renders the claims indefinite because it is unclear which part or size fragment of protein L or cellulose binding domain is referred to. Respectfully, the claims have been amended to recite a "chemically functional fragment thereof." By requiring that the fragment be functional, it is clear that only those fragments capable of binding are covered. Specifically, the claims refer to fragments of protein L that are capable of binding the bindable epitope of the target polypeptide and fragments of cellulose binding domain that are

capable of binding a matrix. That is, the chemical function. Therefore, Applicants respectfully request that this rejection be withdrawn. Moreover, these claims are supported by the Specification as filed, please see the Summary of the Invention pages 1-2.

If Applicants response is inapposite or if Applicants assumptions are incorrect or inappropriate please inform the Applicant. Respectfully, Applicant therefore requests clarification and/or favorable reconsideration of the claims rejected hereunder.

The Rejections Under 35 U.S.C. §112, First Paragraph

New Matter

The Examiner rejects newly entered claims 20 and 26 added by the Applicant in its last response on November 5, 2002 under 35 USC § 112, first paragraph as introducing new matter. Respectfully, Applicant requests that any requirement for canceling the added material specified by the Examiner as "new matter" be withdrawn for the reasons set forth below.

It appears that the Examiner has objected to the insertion of new language reciting a "third binding moiety" on the grounds that specification does not support this inclusion and may broaden the specification without sufficient support in the original disclosure. Respectfully, Applicant points out that each of the original independent claims recited "multivalent" [claims 1, 5, 11, 12, 16, 17] as originally written, and that dependent claims 4, 10 and 15 also recited "multivalent." In addition, the Summary of the Invention introduces the "multivalent" nature of the target molecule on page 1 of the Specification. The Specification also contains over 150 references to a 'multivalent' target polypeptide. Of these it is only in a preferred embodiment(s) of the current invention that recite a target polypeptide produced by the method of the invention that contain only a first and a second binding moiety. (See page 5 of the specification, in the Summary of the Invention).

Respectfully, the Examiner is also reminded that the Inventor is allowed "to be his own lexicographer," and that if this verbal license leads to any ambiguity the claims are to be construed "in connection with the other parts of the..patent application." Autogiro Co. of America v. United States, 384 F.2d 391 (Ct. Cl. 1967).

As the definitions below demonstrate, the underlying theme of the entire application is the production and use of a "multivalent" polypeptide. In this sense the term multivalent means more than one, alternatively understood as two or more. In addition, it is generally understood by Applicants that in the field that binding moiety means:

> "A part or portion of a molecule, generally complex, having a characteristic chemical or pharmacologically active property." Here the chemical trait of note is binding to another molecule or portion thereof. *See*, (**DICTIONARY OF SCIENTIFIC AND TECHNICAL TERMS**, 5th ed., (1994) Sybil P. Parker edit., publ. McGraw-Hill p. 1286).

While "multivalent" is equivalent to "polyvalent" in meaning and provides:

> "[IMMUNOL] Of antigens, having many combining sites [*sic* binding sites] or determinants" Here having many possible binding sites. *See*, (**DICTIONARY OF SCIENTIFIC AND TECHNICAL TERMS**, 5th ed., (1994) Sybil P. Parker edit., publ. McGraw-Hill pp. 1546 and 1311).

Therefore, use of the terms "multivalent" in reference to "binding moieties" should be given their understood meaning in the field, that is, the production of polypeptides of interest that contain within them multiple binding sites (e.g., more than one).

Respectfully, when this understanding is applied to the language of the instant application without modifying language to a 'first' and 'second' binding moiety it becomes clear that Applicant did not enter any new matter in the amendment of 2/7/2003 and that the recitation of "third binding moiety" is supported by the claims and specification as originally filed.

Moreover, the nature of the instant specification and its disclosure provide far more than is required for claims in which the disclosure of a genus (i. e. "multivalent") leads to the claiming of a species (i.e. "third binding moiety"). Ex Parte Westphal, 26 USPQ2d 1858, 1860 (B.P.A.I. 1992)(only requiring implicit description, which is amply provided here). Also as previously stated the nature of the molecules claimed such as, protein L, the cellulose binding domain, antibodies specificities etc., also indicate a potential multivalent polypeptide of interest.

Respectfully, reconsideration is requested. Should the Examiner maintain her rejection Applicant retains its rights to appeal or petition this decision to the Board of Patent Appeals and Interference's. Reconsideration and withdrawal of the rejection is respectfully requested.

Functional Fragment

Claims 9, 10, 21, 22, 27 and 28 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the Applicants, at the time the application was filed, had possession of the claimed invention.

The Examiner has rejected the use of the language "functional fragment thereof" in reference to specific proteins such as the cellulose binding domain, protein L, and various antibodies as unsupported by the specification. Generally, therefore the Examiner is averring that while the sequences of specific proteins may be known, and that their respective pharmacological or chemical activities may be known the knowledge of how to retain this chemical/biological activity in what is essentially a fusion protein with less than a whole protein sequence was not known by the prior art. To this the Applicants fundamentally and vehemently disagree. For clarification of function Applicant has amended the independent base claims or the important dependent claims of note to recite "chemically functional fragment." More specifically, the Applicants also point out that the functional aspect of the proteins of note is their use as tools for purification. That is, the only physiological trait that they needed to retain was their ability to be recognize certain bindable epitopes and be useful in known laboratory protocols or processes for purification purposes. This implicit limitation also limits the claims and limits the language "chemically functional fragment" thereof.

In addition, Applicants point to the prior art and point out that in making the determination as to whether the disclosure requirement is satisfied, the person(s) *skilled* in the art are *presumed* to be aware of all of the relevant literature, including trade publications, textbooks, technical journals, and U.S. patents contemporaneous with the filing of this patent. Whereupon, the disclosure of a relevant discovery, and subsequent allowance as a patent, would then provide a variety of potential uses for those skilled in the art, as mentioned above. The following citations demonstrate this awareness in the prior contemporaneus art relative to some of the functional aspects of fusion proteins changed to aid in those purification efforts contemplated by the invention:

Factor X fusion proteins: improved production and use in the release in vitro of biologically active hirudin from an inactive alpha-factor-hirudin fusion protein.
Guarna MM, *et al.*, Protein Expr Purif. 2000 Nov;20(2):133-41.

Expression, immobilization, and enzymatic characterization of cellulose-binding domain-organophosphorus hydrolase fusion enzymes.
Richins RD, *et al.*, Biotechnol Bioeng. 2000 Sep 20;69(6):591-6.

Expression, purification and applications of staphylococcal protein A fused to cellulose-binding domain.
Shpigel E, *et al.*, Biotechnol Appl Biochem. 2000 Jun;31 (Pt 3):197-203.

Moreover, with regard to the nature of the specification in the instant matter, the uses therein disclosed need not be apparent to everyone, all that is required is that enablement, and the potential usefulness of the discovery is communicated to the skilled artisans of the relevant technology. Given the above citations, available to all workers in the field, the Applicants maintain that any needed teachings were sufficiently performed in the specification. This along with the Federal Circuit's repeated assertions that in the field of biotechnology the level of skill in the art is necessarily a high one, indicates that the enablement requirements for the instant claims be determined not by the public at large but by scientists already trained in many of the basics of the technology and well-versed in standard protocols. Ajinomoto Co., Inc. v. Archer-Daniels-Midland Co., 228 F.3d 1338, 1340 (Fed. Cir. 2000)("Patents, however, are written to enable those skilled in the art to practice the invention, not the public"); Enzo Biochem v. Calgene, Inc., 188 F.3d 1362 (Fed. Cir.1999); *and see*, Enzo Biochem v. Gen-Probe, Inc., 296 F.3d 1316, 1324, 63 USPQ2d 1609, 1613 (Fed. Cir. 2002). Therefore, the Examiners rejection of the claims 9, 10, 21, 22, 27 and 28 under 35 U.S.C. § 112, first paragraph, is overcome, reconsideration is requested. Webster Loom Co. v. Higgins, 105 U.S. 580, 26 L.eD. 1177, 1179 (1882).

New claims 31 through 36, being dependent upon and further limiting independent amended claims 5 and 12 (as the case may be), should also be allowable for that reason, as well as for the additional recitations they contain. Applicants respectfully request favorable consideration of these new claims under 35 U.S.C. § 112, first paragraph in view of the above amendments and remarks.

The Rejection Under 35 U.S.C. §112, Second Paragraph

Claim 25

Claim 25 was rejected under 35 U.S.C. §112, second paragraph for being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. The objection has been addressed through a specific amendment to the claim to clarify, particularly point out, and distinctly claim the subject matter of the invention. Respectfully this rejection is traversed. The pending claim is now believed to comply with the provisions of 35 U.S.C. § 112, second paragraph. Thus, the Examiners rejection based on §112, second paragraph is believed to be traversed. Reconsideration is respectfully requested.

New claims 31 through 36, being dependent upon and further limiting independent amended claims 5 and 12 (as the case may be), should also be allowable for that reason, as well as for the additional recitations they contain. Applicants respectfully request favorable consideration of these new claims under 35 U.S.C. § 112, second paragraph in view of the above amendments and remarks.

The Rejection Under 35 U.S.C. §103(a)

Cheng et al., Schwarz et al., Radford et al., Wagner et al., Vola et al., Meade et al., and Nujiens et al.,

Amended claims 5, 6, 8-10, 12-14, 21-25 and 27-30 stand under 35 U.S.C. §103(a) as being unpatentable over the Cheng *et al.*, reference in view of Schwarz *et al.*, Radford *et al.*, Wagner *et al.*, Vola *et al.*, Meade *et al.*, and Nujiens *et al.* The rejection of the claims, as amended, is respectfully traversed.

The basic considerations which apply to obviousness rejections under MPEP § 2141 are as follows:

(1) the claimed invention must be considered as a whole;

(2) the references must be considered as a whole and must knowingly suggest the desirability and thus the obviousness of making the combination;

(3) the references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and

(4) the reasonable expectation of success is the standard by which obviousness is determined.

When the prior art itself fails to meet even one of the above criteria the cited art does not satisfy 35 U.S.C. § 103(a) and prevents the establishment of the required *prima facie* case of obviousness by the Examiner. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992); In re Rijckaert, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). As pointed out below, the prior art not only fails to provide the suggestion, or incentive to combine but also fails to provide any reasonable expectation of success for the piecemeal combination of the prior art into something resembling the instant invention.

Cheng et al.,

The Cheng *et al.*, patent teaches purifying a polypeptide from a mixture using an antibody. Respectfully, Cheng does not provide for altering the sequence of transgenically produced molecule, does not discuss fusion proteins, does not discuss multivalent binding moieties, and does not discuss any modifications to the structure or amino acid sequence of an antibody or other polypeptide. This lack of guidance, lack of anything resembling "teaching" the invention is clear. Given this, and the controlling precedent cited above not only fails to render obvious the invention it also fails to make itself available for combination as anything resembling analogous art.

Moreover, Cheng *et al.*, fails to provide or teach the following:

a) milk or similar bodily derived substance;

b) purification of a transgenically derived molecule using a second transgenically derived molecule; or

c) modifying a polypeptide sequence to make purification easier through the use of known binding domains.

Respectfully, these deficiencies are not remedied by the piecemeal application of the other citations provided by the Examiner. That is, though the Cheng *et al.*, reference and other citations are tasked to providing a solution to the same or similar problem the solutions each provides is significantly different and either simply would not be combined by a artisan in one field (purification/ chromatography/ solution procession) with the art of another field (transgenic molecular biology/ genetic engineering) such that they are not analogous art available for combination or alternatively offer so many other possibilities toward some purification scheme as to lack and direct or purposeful teaching that could usefully be combined.

Schwarz et al,

Schwarz *et al.*, does not provide what Cheng *et al.*, lacks. Schwarz presents the use or bacteria derived protein L and its use in purification schemes. More specifically, Schwarz et al., presents the use of protein L in the purification schemes for antibodies. It does not teach anything resembling the construction and purposeful manipulation of transgenic mammals or the directed alteration of target polypeptides for later biologic production and final production in milk or a biologically derived liquid feedstream. Likewise it fails to mention, suggest or teach milk as a reaction mixture. For these reasons it to essentially functions as non-analogous art and is unavailable for any combination. Moreover, the patent suggests that the methods provided therein are necessary and sufficient for the purification methods provided. That is, no other teachings are suggested. Respectfully, therefore, it is clear that this citation simply does not provide any suggestion for combination or alternate modes of purification that would make it available to combine with other prior art. Nor can it teach (due to its remoteness in time) any combination with Cheng *et al.*,.

Thus, neither of the amended independent claims 5 and 12 can be obvious over Schwarz *et al.*, either alone or in combination with Cheng *et al.*, given these remarks and those already provided, nor can any claims dependent upon them.

Radford et al.

Radford *et al.* also fails to provide what the Cheng *et al.*, and Schwarz references lack. In fact Radford *et al.*, essentially only provides a citation discussing the cellulose binding domain

(CBD) and the possibility of adding this domain to a polypeptide of interest. In this sense it catalogs what is known in the prior art about the CBD and offers its use for purification schemes -but offers little else. It does not suggest a multivalent polypeptide, transgenic mammalian production, or elution of these molecules from a biologically derived feedsteeam. Therefore, Radford offers little to the combination of Cheng *et al.*, and Schwarz – even if it could be combined with them.

Similar arguments and recitations can be made with each of the Wagner, Vola, Meade, and Nuijens citations. Each in turn fails to suggest a combination or is simply non-analogous art. With the unavailability of Cheng, Schwartz and Radford for combination as non-analogous art or simply through lack of any teaching to combine the other citations cannot maintain anything resembling an obviousness rejection.

The present invention, as recited in amended independent claims 5 and 12 offers the benefits of a novel structural methods, transgenic production and a different method of polypeptide purification. If the invention as recited were obvious, then those skilled in the art would have long since adopted this invention. However, according to the art of record, those skilled in the art have not adopted the present invention, and therefore do not get the benefit of the invention. Therefore, it is proposed that independent claims 5 and 12 and those claims in turn dependent upon them, cannot be obvious.

Dependent claims 6, 8-10, 13-14, 21-25 and 27-30 being dependent upon and further limiting independent amended claims 5 and 12 should also be allowable for that reason, as well as for the additional recitations they contain. Applicants respectfully request reconsideration of the rejection of claims 1-26 under 35 U.S.C. § 103(a) in view of the above amendments and remarks.

New claims 31 through 36 have similar limitations to those discussed above. As they retain all the elements of the amended base claims from which they depend they should be allowable for this reason, as well as for the additional recitations they contain. Applicants therefore respectfully request favorable consideration claims 27-44 under 35 U.S.C. § 103(a), in view of the above amendments and remarks.

Respectfully, with the above references the Examiner is establishing the use of a broad spectrum of protocols and information briefly recapitulating the entirety of the prior art with regard to molecular biology and some purification chemistry and pulling out elements of that

prior art that may *arguendo* compare with the current invention. However, as stated above, the information provided by these citations simply fails to provide any quantifiable suggestion of a combination to effect the instant claims. The Examiner states that at the time of the invention it would have been obvious to one of ordinary skill in the art to practice all of the relevant techniques of the disparate citations together. However, it must be remembered that "obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching suggestion or incentive supporting the combination." In re Geiger, 815 F.2d 686, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987). Not only is there is no suggestion for this combination in the prior art, in addition, any combination of the references simply does not produce the invention as claimed in claims 5, 6, 8-10, 12-14, 21-25 and 27-30.

Going further, the number of citations necessarily cobbled together by the Examiner is itself testimony to the patentability of the instant claims. Yamanouchi Pharm. Co. v. Danbury Pharmacal, Inc. 231 F.3d 1339; 56 U.S.P.Q.2D 1641 (Fed. Cir. 2000). As stated above, the fusion proteins, reaction mixtures, purification schemes, and production elemetns of the independent claims contain a novel recombinant gene sequences and are not found in a natural state or prior art purification methods. The claims provided by the Applicants represent the product of long laboratory experimentation. If they could be rendered obvious by a simple recitation of similar procedures, very little in the field of biotechnology would be patentable. To defeat the instant claims the Examiner must provide more than an odd collection of references that recast known technology. The Examiner must provide references that knowingly suggest the precise combination of protocols, tests, and principles, which will put the invention in the hands of the public. Applicant respectfully suggests that the Examiner has not provided these references.

In addition, it must be respectfully reiterated that each of the citations provided above fail to recognize, expressly or implicitly, any need, possibility or benefit of combining their disparate teachings in such a way that they might then read on the instant claims. Absent some teaching, suggestion, or incentive supporting this combination, a teaching that is simply not present in any of the citations provided by the Examiner, the references are incapable of supporting a obviousness rejection under § 103(a). Carella v. Starlight Archery, 231 U.S.P.Q. 644 (Fed. Cir. 1986).

It should also be pointed out that it is well settled law that there is no longer a "flash of genius" requirement for patentability. That is, patentability does not rest on the development of

new technology that completely eliminates prior art problems and difficulties, rather, patents can and should be issued to stepwise improvements in technology that are novel and otherwise meet the standards of the Patent Code. Cuno Eng'g Corp. v. Automatic Devices Corp., 314 U.S. 84, at 91 (1941) (proclaiming the "flash of genius" standard later abolished by institution of the current United States Patent Code of 1952); Graham v. John Deere Co., 383 U.S. 1, at 15-16 (1966) (Specifically overruling Cuno) (as applied here, the complete inhibition of the myriad difficulties associated with the production of a chemically active fusion protein/target polypeptide in a transgenic mammal production platform contemplating a purification methodology).

The Examiner must provide references that ***knowingly*** suggest the combination of protocols, tests, or principles, which will lead to the invention to be rendered obvious, and read upon its claims. The Examiner has not provided these references. Rather the Examiner has stated that the instant claims are "as a whole..*prima facie* obvious". Without more, this is a classic reproduction of the invention from improper hindsight, which cannot be used to negative patentability or establish the required case of *prima facie* obviousness. In re Dillon, 919 F.2d at 696, 16 USPQ2d at 1904 (Fed. Cir. 1990) (*en banc*); In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988); In re Geiger, 815 F.2d 686, 2 USPQ2d 1276, 1278 (Fed. Cir.1987).

Respectfully, it is thus the objective measure of obviousness that the prior art cited of record is incapable of supporting, thus preventing the maintenance of a 35 U.S.C. §103(a) rejection. Appellants therefore respectfully request the withdrawal of the Rejection of amended claims 5, 6, 8-10, 12-14, 21-25 and 27-30 under 35 U.S.C. §103(a) as being unpatentable over Cheng et al, in view of Schwarz *et al.*, Radford *et al.*, Wagner *et al.*, Vola *et al.*, Meade *et al.*, and Nujiens *et al.*

New claims 31 through 36, being dependent upon and further limiting independent amended claims 5 and 12 (as the case may be), should also be allowable for that reason, as well as for the additional recitations they contain. Applicants respectfully request favorable consideration of these new claims under 35 U.S.C. § 103(a) in view of the above amendments and remarks.

The Commissioner is authorized to charge any fee which may now or hereafter be due for this divisional application to GTC Biotherapeutics' Deposit Account No. 502092.

Applicants respectfully submit that the pending claims of this application are in condition for allowance, and that this case is now in condition for allowance of all claims therein. Such action is thus respectfully requested. If the Examiner disagrees, or believes for any other reason that direct contact with Applicant's attorney would advance the prosecution of the case to finality, the Examiner is invited to telephone the undersigned at the number given below.

Early and favorable action is earnestly solicited.

Respectfully Submitted,

Date: 8/7/03

By: Byron V. Olsen

Byron V. Olsen, Reg. No. 42,960
ATTORNEY FOR APPLICANTS
GTC Biotherapeutics, Inc.
175 Crossing Blvd., Suite 410
Framingham, MA 01702
Tel. # (508) 370-8150
Fax # (508) 370-3797

Claims Appendix

Current Recitations of Existing Claims:

5. A method of obtaining a target polypeptide having a bindable epitope from a product, the method comprising:

contacting a product which comprises a target polypeptide having a bindable epitope with a transgenically produced multivalent binding polypeptide, wherein the transgenically produced multivalent binding polypeptide comprises a first binding moiety which specifically binds the bindable epitope of the target polypeptide and a second binding moiety which specifically binds a matrix, to thereby provide a reaction mixture;

contacting the reaction mixture with a matrix which specifically binds the second binding moiety of the multivalent binding polypeptide;

removing reaction mixture which does not bind to the matrix, to thereby obtain the target polypeptide from the product; and

wherein the reaction mixture is substantially fluid.

6. The method according to claim 5, further comprising eluting the target polypeptide from the matrix.

8. The method according to claim 5, wherein the target polypeptide is an antibody.

9. The method according to claim 8, wherein the first binding moiety of the transgenic multivalent binding polypeptide is protein L or a chemically functional fragment thereof.

10. The method according to claim 9, wherein the second binding moiety of the transgenic multivalent binding polypeptide is a cellulose bind domain (CBD) or a chemically functional fragment thereof.

12. A method of obtaining a target polypeptide having a bindable epitope from the milk of a

first non-human transgenic mammal, the method comprising:

contacting milk which comprises a target polypeptide having a bindable epitope with a transgenically produced multivalent binding polypeptide, wherein the multivalent binding polypeptide comprises a first binding moiety which specifically binds the bindable epitope of the target polypeptide and a second binding moiety which specifically binds a matrix, to thereby provide a reaction mixture;

contacting the reaction mixture with a matrix which specifically binds the second binding moiety of the multivalent binding polypeptide;

removing reaction mixture which does not bind to the matrix, to thereby obtain the target polypeptide from the milk;

wherein the reaction mixture is substantially fluid; and,

wherein the transgenically produced multivalent binding polypeptide is produced in milk from a second non-human transgenic mammal.

13. The method according to claim 12, further comprising eluting the target polypeptide from the matrix.

14. The method of claim 12, wherein the target polypeptide is a transgenically produced polypeptide.

19. The system according to claim 2, wherein the transgenically produced multivalent polypeptide further comprises a third binding moiety and the third binding moiety is capable of removing the bindable epitope from the target polypeptide.

20. The method according to claim *5,* wherein the transgenically produced multivalent polypeptide further comprises a third binding moiety and the third binding moiety is capable of removing the bindable epitope from the target polypeptide.

21. The method of claim 5, wherein the first binding moiety of the multivalent binding

polypeptide is an antibody or functional fragment thereof which binds the bindable epitope of the target polypeptide.

22. The method of claim 5, wherein the second binding moiety of the multivalent binding polypeptide is a cellulose binding domain (CBD), or a chemically functional fragment thereof.

23. The method of claim 5, wherein the target polypeptide is a receptor and the first binding moiety of the multivalent binding polypeptide is a ligand which binds the bindable epitope of the receptor.

24. The method of claim 5, wherein the first binding moiety of the multivalent binding polypeptide is a receptor which binds the bindable epitope of the target polypeptide.

25. The method according to claim 12, wherein the transgenically produced multivalent binding polypeptide is produced in the milk of a second non-human transgenic mammal.

26. The method of claim 12, wherein the transgenically produced multivalent polypeptide further comprises a third binding moiety and the third binding moiety is capable of removing the bindable epitope from the target polypeptide.

27. The method of claim 12, wherein the first binding moiety of the multivalent binding polypeptide is an antibody or chemically functional fragment thereof which binds the bindable epitope of the target polypeptide.

28. The method of claim 12, wherein the second binding moiety of the multivalent binding polypeptide is a cellulose binding domain (CBD), or a chemically functional fragment thereof.

29. The method of claim 12, wherein the target polypeptide is a receptor and the first binding moiety of the multivalent binding polypeptide is a ligand which binds the bindable

epitope of the receptor.

30. The method of claim 12, wherein the first binding moiety of the multivalent binding polypeptide is a receptor which binds the bindable epitope of the target polypeptide.

Please add claims 31-36

31. The method of claim 5, wherein said multivalent polypeptide is used in an ELISA format.

32. The method of claim 6, wherein said target polypeptide is purified from the reaction mixture to a composition that is more than 90% pure.

33. The method of claim 5, wherein said reaction mixture is semi-solid

34. The method of claim 12, wherein said multivalent polypeptide is used in an ELISA format.

35. The method of claim 12, wherein said target polypeptide is purified from the reaction mixture to a composition that is more than 90% pure.

36. The method of claim 12, wherein said reaction mixture is semi-solid.